

Low-Dose Effects of Endocrine Disruptors, with Laura Vandenberg

Ashley Ahearn

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Reproduction, growth, behavior, and sleep patterns are just a few of the bodily functions controlled by hormones. Researchers around the world are examining what happens if chemical substances we're exposed to in our daily lives interrupt or imitate natural hormonal messages. The body of scientific evidence so far suggests that even at very low doses, exposures to endocrine disruptors may have very real effects, and that low-dose effects may disappear at higher doses, giving an illusion of safety if chemicals are not tested at low-enough doses. In this podcast, host Ashley Ahearn talks with Laura Vandenberg about her recent review of the evidence on health effects of low-dose exposures to endocrine disruptors.

AHEARN: It's *The Researcher's Perspective*. I'm Ashley Ahearn.

Reproduction, growth, behavior, sleep patterns—what do they have in common? These are just a few of the natural functions in our bodies that are controlled by hormonal messages sent by the endocrine system.

So, what happens if chemical substances we're exposed to in our daily lives interrupt or imitate those natural hormonal messages?

That's a question researchers around the world are trying to answer. And the body of scientific evidence so far suggests that even at very low doses, exposures to these so-called endocrine disruptors may have very real effects. What's more, low-dose effects may disappear at higher doses, giving an illusion of safety if chemicals are not tested at low-enough doses.

An editorial in the April issue of *EHP* takes a look at a comprehensive review of the research on this subject.ⁱ

Laura Vandenberg coauthored the original review, which appeared in the journal *Endocrine Reviews*.ⁱⁱ It's the largest effort in over a decade to examine the literature on low-dose exposures to endocrine disruptors and the possible human health outcomes. She's a postdoctoral fellow at the Center for Regenerative and Developmental Biology at Tufts University.

Hi, Dr. Vandenberg.

VANDENBERG: Hi, Ashley. Thanks for having me.

AHEARN: We're exposed to endocrine disruptors every day. What are they, and where are they found?

VANDENBERG: These are chemicals that we come into contact with in pretty much every aspect of our daily lives. So as soon as we get out of the bed and get into the bathroom we're being exposed to them in things that we use as personal care products, as cosmetics. When we're putting together our breakfasts, there are chemicals that are found on our food or in food packaging. When we get in our cars to go to work, there are chemicals that are found in the upholsteries or in the particulates that we're exposed to in air from diesel exhaust. They're chemicals that we use on our lawns to keep our lawns looking nice and green, and they're chemicals that we use in our homes to keep bugs out and to keep things looking shiny and clean. So [in] pretty much every aspect of our daily lives we're encountering chemicals that can mimic or block the actions of hormones in our body.

AHEARN: Why did you do this study, and how many studies did you review for this?

VANDENBERG: This [type of review] was originally done back in 2001 and 2002 by the National Toxicology Program together with NIEHS,^{iii,iv} and they were asking at the time, is there evidence that endocrine disruptors have actions at low doses? We wanted to go back and ask, is this something that's common for all endocrine disruptors, to act at low doses? So we were trying to look at as many chemicals as possible at once, and really that was the first time anyone had thought to do that because most researchers focus on a single chemical at a time.

So we identified 28 chemicals with cutoffs for low doses^v and then found that there were effects below that low-dose cutoff, so essentially every chemical that we looked at, that we knew what a "low dose" would be, had an effect in that range of low doses.

AHEARN: Was that what you were expecting to find?

VANDENBERG: From an endocrinologist's point of view, this actually isn't terribly surprising. Hormones work in the body in the part-per-billion or part-per-trillion level, so we're talking about maybe a teaspoon in an Olympic-sized swimming pool. They're supposed to work at low doses, so looking at chemicals that would mimic the actions of hormones I did expect that we would find actions of these chemicals at low doses.

What was perhaps surprising is that [for] every chemical that we looked at that we could find a low-dose cutoff, if it had been studied at low doses it had an effect at low doses.

AHEARN: Dr. Vandenberg, what kind of effects in the general population might be associated with exposure to these low doses of endocrine disruptors, and how strong is the evidence for these effects that we may or may not be seeing already in the population?

VANDENBERG: Some of the trouble with looking at human populations is really that if we were looking at a pharmaceutical we could look at people who were exposed to the chemical and people who weren't exposed to it, those who had purposefully taken it and those who hadn't taken it. With something like an endocrine disruptor we're all being exposed to these chemicals all the time, so it's very hard to find a population to compare those of us who are exposed to because there is no control population. In that case, epidemiologists have to very carefully look and compare exposures for who's exposed to less of a chemical and who's exposed to more of a chemical.

And some of those studies really are suggesting that endocrine disruptors could be linked to human health effects like infertility, diabetes and obesity, other aspects of metabolic syndrome,^{vi} cardiovascular disease, and on and on and on. Some of the diseases that have been implicated are really concerning like Parkinson's disease, autism, ADHD [attention deficit/hyperactivity disorder]—so these are the kinds of diseases that we're seeing that are increasing in prevalence in the population, and whether or not endocrine disruptors are responsible or playing a role is a real serious concern.

AHEARN: But this isn't to say that endocrine disruptors are going to be the great explainer catch-all for these problems that we see in the population. I mean, some of these effects are extremely subtle, and so subtle that we really can't say for sure whether they're even a concern or not. Can you talk a little bit about that?

VANDENBERG: Some of the effects of endocrine disruptors on animals are slight changes that we see in the development of animals, and how they relate to human diseases, in some cases, is not very clear. In other cases it is quite clear. So in our review, we examined the literature connecting BPA exposures—that's bisphenol A, the plastic chemical that's been studied incredibly well—and its role in affecting the mammary gland of rodents that are exposed. And what we looked at were all of the studies that had looked at BPA and the mammary gland, whether they found an effect or they didn't find an effect. Overwhelmingly, those studies suggest that BPA affects the development of the mammary gland. It can induce precancerous and cancerous lesions, and it makes those animals more sensitive to chemical carcinogens.

So is this evidence that BPA could be doing the same thing in humans? There certainly is concern for that, but how would you study that in humans? We would need to go to very young people and know how much BPA they were exposed to in the womb and then follow them for decades. And there are researchers who are starting to try to do that kind of experiment, but we're talking about results that we won't have for another 50 years.

AHEARN: Dr. Vandenberg, this is a really contentious subject to research, and I wonder, how have you observed scientists in your field navigating that sort of risky terrain of being branded an “activist scientist”?

VANDENBERG: Well, for me I think it’s very important to keep the distinction between what the data shows and public opinion about data, so a lot of change that’s been made, particularly in consumer products, has been driven by what consumers think. So, for example, BPA was removed from baby bottles by the industry not because of any regulatory action in most cases, but because that’s what consumers wanted. The real question for me as a scientist is, is there sufficient evidence to suggest that BPA should be removed from baby bottles? In that case, I think that there was and there is. In fact, I think that there’s sufficient evidence that BPA should not be in contact with food, but that’s, that’s a very scientific opinion that’s based on looking at hundreds of animal studies and not based on a gut reaction on what I think about BPA or any other particular chemical.

AHEARN: What’s next for you, Dr. Vandenberg? What are you excited to explore further?

VANDENBERG: I think that one of the really important aspects of this work that needs to be looked at and studied is understanding how chemicals act when they’re in mixtures. So again, a lot of this work has been done by looking at a single chemical at a time, but that’s not how humans are actually exposed to chemicals. We’re exposed every time we eat something to several chemicals at a time, and we really have very little evidence about how these chemicals are acting together. Do two estrogens act additively? Does an estrogen and an antiestrogen counteract each other? Do they cross each other out? The few studies that have been done suggest that those sort of simple mathematical predictions don’t actually reveal what’s happening in the biology of the animal, and that’s what I want to explore. That’s where I want to go.

AHEARN: Well, Dr. Vandenberg, thank you so much for joining me today.

VANDENBERG: Thank you.

AHEARN: Laura Vandenberg is a postdoctoral fellow at the Center for Regenerative and Developmental Biology at Tufts University.

And that’s *The Researcher’s Perspective*. I’m Ashley Ahearn. Thanks for downloading!

Ashley Ahearn, host of *The Researcher’s Perspective*, has been a producer and reporter for National Public Radio and an Annenberg Fellow at the University of Southern California specializing in science journalism.

References and Notes

ⁱ Birnbaum LS. Environmental chemicals: evaluating low-dose effects. *Environ Health Perspect* 120(4):A143–A144 (2012); <http://dx.doi.org/10.1289/ehp.1205179>.

ⁱⁱ Vandenberg L, et al. Hormones and endocrine-disrupting chemicals: low-dose effects and nonmonotonic dose responses. *Endocrine Rev*; doi:10.1210/er.2011-1050 [online 14 Mar 2012].

ⁱⁱⁱ Melnick R, et al. Summary of the National Toxicology Program's report of the endocrine disruptors low-dose peer review. *Environ Health Perspect* 110(4): 427–431 (2002); PMID:1240807.

^{iv} NTP. National Toxicology Program's Report of the Endocrine Disruptors Low Dose Peer Review. Research Triangle Park, NC:National Toxicology Program/National Institute of Environmental Health Sciences (2001). Available: <http://ntp.niehs.nih.gov/ntp/htdocs/liason/LowDosePeerFinalRpt.pdf> [accessed 23 May 2012].

^v The low-dose cutoff for each chemical was defined by the investigators as “the lowest dose tested in traditional toxicology studies, or doses in the range of human exposure, depending on the data available.”

^{vi} Metabolic syndrome is a cluster of conditions that raise the risk for health problems such as heart disease, type 2 diabetes, and stroke. To be diagnosed with metabolic syndrome, at least three of the following risk factors be present: 1) excess fat in the stomach area (having an “apple shape”), 2) high triglycerides, 3) low HDL (“good”) cholesterol, 4) high blood pressure, and 5) high fasting blood sugar.